

# Highly Selective Syntheses of Coniferyl and Sinapyl Alcohols

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## Introduction

Coniferyl and sinapyl alcohols are the building blocks for lignin. Lignin is the plant cell wall polymer that provides the plant with structural integrity, water transport, and defense. It is also the polymer that limits the utilization of wall polysaccharides by ruminants, and is the component that must be removed in chemical pulping for paper production. Coniferyl and sinapyl alcohols are used in a variety of studies relating to forage chemistry as well as in wood chemistry.

A number of synthetic methods for them have been developed; every year in these Research Summaries, we come up with a better method! The alcohols were originally obtained from their corresponding cinnamates by lithium aluminum hydride reduction in moderate yield. Recently, more selective reducing agents such as diisobutylaluminum hydride have been used to improve selectivity and allow conversion of unprotected 4-hydroxycinnamates to alcohols. Other approaches have also been reported. All of them suffer from either low yields, undesirable contaminants, or difficult in handling reagents. Normally, coniferyl or sinapyl alcohol prepared from these methods is contaminated with varying amounts of the saturated alcohol which is hard to separate even by recrystallization. Now that the aldehydes are commercially available, their reductions provide the easiest way to prepare the hydroxycinnamyl alcohols. However, coniferyl or sinapyl alcohol prepared by the recently developed method, in which sodium borohydride ( $\text{NaBH}_4$ ) is used as the reducing agent, is still contaminated with saturated alcohols. Here we report a facile and highly selective method to synthesize coniferyl or sinapyl alcohol from coniferaldehyde or sinapaldehyde by sodium triacetoxyborohydride ( $\text{NaBH}(\text{OAc})_3$ ) reduction in ethyl acetate in excellent yields. The method is simple and safe enough that non-chemists can readily make the requisite monolignols.

## Experimental Procedures

### Preparation of Sodium Triacetoxyborohydride

To  $\text{NaBH}_4$  (74 mg) suspended in ethyl acetate (15 mL) and cooled with an ice water bath, was added glacial acetic acid (3.05 eq) by syringe over about 5 min. Stirring was continued for another 5 min. until a clear solution was formed. The solution is the ready-to-use reducing agent. For large scale (3.5 g), the addition of acetic acid was performed dropwise over about 30 min and stirring was continued for a further 30 min.

### Coniferyl Alcohol **2a**

Coniferaldehyde **1a** (134 mg, 0.753 mmol) was added to sodium triacetoxyborohydride (3.0 eq) in ethyl acetate, prepared as above. The reaction was monitored by TLC (5%  $\text{CH}_3\text{OH}$  in  $\text{CH}_2\text{Cl}_2$ ). TLC showed that the starting material completely disappeared in 7 h. However, the reaction mixture was kept overnight, then diluted with ethyl acetate and quenched with water (20 mL). The organic phase was separated and the water fraction was extracted with ethyl acetate (2 x 20 mL). The combined ethyl acetate was washed with water (20 mL), sat.  $\text{NH}_4\text{Cl}$  (20 mL) and dried over  $\text{MgSO}_4$ . Evaporation of the solvent gave a light yellow syrup which still contained acetic acid. The residual acetic acid was removed by coevaporation with ethanol.  $^1\text{H NMR}$  and GC of this crude **2a** (132 mg, 97%) showed no detectable 1,4-reduction product (detectability limit < 0.05%). Crystallization from  $\text{CH}_2\text{Cl}_2$ /petroleum ether gave **2a** as pale yellow plates (95 mg, 70%), mp 77.2-77.9 °C. For large scale preparation (5 g), after addition of coniferaldehyde **1a**, the mixture was stirred overnight (~10 h) at room temperature. Work up as above afforded crude **2a** without any 1,4-reduction product detectable by GC. Crystallization from  $\text{CH}_2\text{Cl}_2$ /petroleum ether led to pure **2a** as pale yellow plates in 77% yield.

## Sinapyl Alcohol 2b

Sinapaldehyde **1b** (130 mg, 0.62 mmol) was reduced as described for **1a** to yield crude sinapyl alcohol **2b** as pale yellow syrup (120 mg, 91%). Again, no dihydrosinapyl alcohol could be detected by NMR or GC. For large scale preparation, sinapaldehyde **1b** (5.0 g, 24.0 mmol) was reduced overnight as described for **1a** to yield crude sinapyl alcohol **2b** as a pale yellow syrup (4.85 g, 96%). Crystallization of sinapyl alcohol is difficult. The product produced by this method is suitable for use without further purification.

## Discussion

Sodium borohydride is a versatile and relatively mild reducing agent generally used for the reduction of aldehydes and ketones. However, reduction of conjugated aldehydes and ketones with sodium borohydride is highly solvent dependent and generally does not result in useful regioselectivity. It is not surprising that coniferyl alcohol prepared by sodium borohydride reduction of coniferaldehyde was contaminated with saturated coniferyl alcohol. GC showed that about 3% levels of saturated coniferyl alcohol were obtained when coniferaldehyde was reduced by sodium borohydride in ethyl acetate (Fig. 1).

Sodium (mono- and tri-)acetoxyborohydrides, prepared by adding controlled amounts of acetic acid to sodium borohydride in a solvent, reduced enones and enals in THF more selectively than the parent sodium borohydride.  $\text{NaBH}(\text{OAc})_3$  reduced aldehydes in the presence of ketones.  $\text{NaBH}(\text{OAc})_3$

was chosen for preparing coniferyl and sinapyl alcohols, even though it is weaker in reactivity than sodium monoacetoxyborohydride, because it is commercially available and more easily prepared *in situ*. Coniferaldehyde **1a** and sinapaldehyde **1b** were smoothly reduced to coniferyl alcohol **2a** and sinapyl alcohol **2b** by sodium triacetoxyborohydride, in ethyl acetate with no detectable 1,4-reduction product (Figure 1). The yields were 97% and 92% for **2a** and **2b**, respectively. Coniferyl alcohol **2a** was crystallized from methylene chloride/petroleum ether in 70% yield. Multigram quantities of coniferyl alcohol and sinapyl alcohol were prepared in the same way without any difficulty and coniferyl alcohol was easily crystallized in 77% yield. Attempts to crystallize sinapyl alcohol from methylene chloride/petroleum ether were unsuccessful. We and others have had this difficulty in the past and it is not necessarily indicative of less pure sinapyl alcohol. Crude sinapyl alcohol was pure enough to be used directly for making synthetic lignins or other purposes.

The major advantages of this method are: 1) the reducing agent, sodium triacetoxyborohydride, is either available from commercial sources or easily generated and used directly without requiring particular caution; 2) large scale preparations can be easily accomplished by this method with similar results; and 3) the expected products are prepared in high yields without any 1,4-reduction that produces the saturated alcohols that always exist in previously described methods. The products are used in a variety of studies ultimately aimed at enhancing the utilization of forages and improving sustainability.

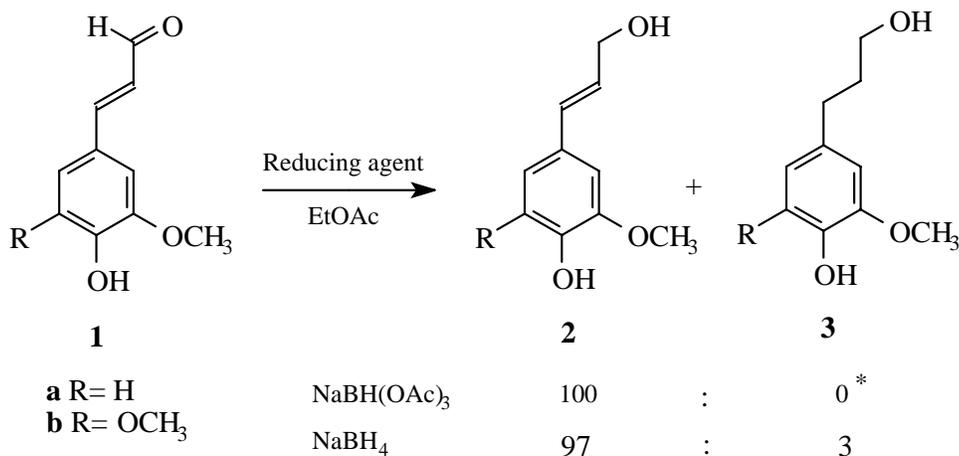


Figure 1. Reduction of coniferaldehyde **1a** and sinapaldehyde **1b**. \*The ratio was measured by GC; **3a-b** were undetectable in products of  $\text{NaBH}(\text{OAc})_3$  reductions.